UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/039,635	01/02/2002	Charles T. Black	YOR9-2001-0319-US1	9290

7590 11/13/2003

McGinn & Gibb, PLLC
Suite 200
8321 Old Courthouse Road
Vienna, VA 22182

EXAMINER	
JOHNSTON, PHILLIP A	
ART UNIT	PAPER NUMBER
2881	

DATE MAILED: 11/13/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/039,635	BLACK ET AL.	
	Examiner	Art Unit	
	Phillip A Johnston	2881	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 September 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-36* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-36* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *02 January 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

Detailed Action

Claims Rejection – 35 U.S.C. 103

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which the subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

2. Claims 1-36 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent Pub. No. 2002/0063212 to Mirkin, in view of Haubold U.S. Patent Pub. No. 2003/0032192, and in further view of Cubbiciotti U.S. Patent Pub. No. 2002/0034757.

Mirkin (212) discloses "dip pen" nanolithography (DPN), wherein DPN is a direct-write, nanolithography technique by which molecules are delivered to a substrate of interest in a positive printing mode. DPN utilizes a solid substrate as the "paper" and a scanning probe microscope (SPM) tip (e.g., an atomic force microscope (AFM) tip) as the "pen". The tip is coated with a patterning compound (the "ink"), and the coated tip is used to apply the patterning compound to the substrate to produce a desired pattern. As presently understood, the molecules of the patterning compound are delivered from the tip to the substrate by capillary transport. DPN is useful in the

fabrication of a variety of microscale and nanoscale devices. The invention also provides substrates patterned by DPN, including combinatorial arrays, and kits, devices and software for performing DPN.

The SPM tip is coated by dipping the tip into a solution of the patterning compound. The solvent is not critical; all that is required is that the compound be in solution. However, the solvent is preferably the one in which the patterning compound is most soluble. Also, the solution is preferably a saturated solution. In addition, the solvent is preferably one that adheres to (wets) the tip (uncoated or coated with an adhesion layer) very well (see above). The tip is maintained in contact with the solution of the patterning compound for a time sufficient for the compound to coat the tip. See Paragraphs [0011] and [0082].

Mirkin (212) also discloses that DPN will be particularly uses for the preparation of combinatorial arrays on the submicrometer scale. An "array on the submicrometer scale" means that at least one of the dimensions (e.g., length, width or diameter) of the sample areas, excluding the depth, is less than 1 mμm. At present, DPN can be used to prepare dots that are 10 nm in diameter.

Each sample area of an array contains a single sample. For instance, the sample may be a biological material, such as a nucleic acid (e.g., an oligonucleotide, DNA, or RNA), protein or peptide (e.g., an antibody or an enzyme), ligand (e.g., an antigen, enzyme substrate, receptor or the ligand for a receptor), or a combination or mixture of biological materials (e.g., a mixture of proteins). Such materials may be

deposited directly on a desired substrate as described above (see the description of patterning compounds in paragraph [0082] above).

FIGS. 9A-C. Schematic diagrams with lateral force microscopy (LFM) images of nanoscale molecular dots showing the "essential factors" for nanometer scale multiple patterning by DPN. Scale bar is 100 nm. FIG. 9A shows a first pattern of 15 nm diameter 16-mercaptohexadecanoic acid (MHA) dots on Au(111) imaged by LFM with the MHA-coated tip used to make the dots. Chemical compounds may be deposited directly on the substrate or may be attached through a functional group present on a patterning compound present in the sample area. As yet another example, each sample area may contain a type of microparticles or nanoparticles. See Paragraphs [0030], [0103] and [0104].

Mirkin (212) further discloses that the tip is also preferably one to which the patterning compound physisorbs only. As used herein "physisorb" means that the patterning compound adheres to the tip surface by a means other than as a result of a chemical reaction (i.e., no chemisorption or covalent linkage) and can be removed from the tip surface with a suitable solvent. Physisorption of the patterning compounds to the tip can be enhanced by coating the tip with an adhesion layer and by proper choice of solvent (when one is used) for the patterning compound. The adhesion layer is a uniform, thin (~10 nm) layer of material deposited on the tip surface which does not significantly change the tip's shape. It should also be strong enough to tolerate AFM operation (force of about 10 nN). See Paragraph [0054]

Mirkin (212) still further discloses a strategy for chemically and physically immobilizing a wide variety of particle types and sizes with a high degree of control over particle placement calls for a soft lithography technique capable of high-resolution patterning, but also with the ability to form patterns of one or more molecules with precision alignment registration. DPN is such a tool. This example demonstrates combinatorial arrays produced by DPN, focusing on the problem of particle assembly in the context of colloidal crystallization. See Paragraph [0201}.

It is implied herein that dipping of the probe tip in solution in accordance with Mirkin (212) is equivalent to dipping the tip apex as recited in Claim 10.

Mirkin (212) as applied above does not disclose the use of synthesized nanoparticles, as recited in Claim 1. However, Haubold (192) discloses that inorganic nanoparticles capable of fluorescence are prepared by a liquid phase synthesis using an organic solvent. First, this gives colloidal solutions of highly crystalline nanoparticles. By using further steps of the preparation method, these nanoparticles in solution can then be precipitated and dried. According to the solvent that is used, the cation source or anion source for the host lattice that are used and, if necessary, whether one or some further cation sources (preferred are metal salts) as doping agent are applied, this then results in desired nanoparticles and in particular properties of the nanoparticles.

Therefore it would have been obvious to one of ordinary skill in the art that the scanning probe microscope apparatus and method of Mirkin (212) can be modified to

use synthesized nanoparticles in accordance with Haubold (192), to coat the probe tip as recited in Claims 1, 10, and 25-28.

Haubold (192) also discloses the use of spherical nanoparticles (as recited in Claims 30-36) in the publication;

"Synthesis of submicron spherical crystals of gadolinium garnets by the glycothermal method", by Inoue, M. et al., in Journal of Materials Science Letters 14 (1995), pp 1303-1305. See Paragraphs [0190]-[0192].

Also according to the Haubold (192) invention, the other components of the solvent mixture are preferably chosen in a way that the boiling point of the mixture lies at a emperature which is sufficiently high to allow the formation of nanocrystals. This temperature is called herein synthesis minimum temperature. The amount of the other components is then high enough allowing the synthesis mixture to keep the nanoparticles that are formed during the synthesis reaction in solution.

Preferred are then such components, which degrade during the reaction process as little as possible. More preferred are components, which allow, after the end of the reaction, to be removed by distillation at reduced pressure without degradation. The distillation should be a simple method as usually employed in the laboratory, e.g. using an oil pump for the vacuum, not better than 0.01 mbar, and a water bath or oil bath providing a distillation temperature not greater than 200.degree. C., which corresponds to approx. 480 Kelvin. See Paragraphs [0101] and [0063]-[0065].

It is implied herein that the removal of solvents in accordance with Haubold (192) is equivalent to the use of a nonvolatile solution, as recited in Claim 26.

Mirkin (212) in view of Haubold (192) as applied above does not disclose the use of an elastomer or an electrochemical solution containing nanoparticles as recited in Claims 26 and 28. However, (757) discloses that proximity-based methods for single-molecule detection include proximal probe methods (e.g., AFM, STM) with reporter molecules (e.g., macromolecules, polymers or preferably nanoparticles or microparticles) to select and isolate one or more aptamers based upon a user-defined selection criterion or setpoint (e.g., target-binding affinity). For example, by varying the size, density, surface charge and/or solubility of reporters conjugated to the target molecule, on the one hand, and random-sequence nucleic acids, on the other, an individual aptamer or group of aptamers can be selected with desired binding strength. The affinity or binding strength required for aptamer-dependent assembly and maintenance of paired reporter particle complexes increases with the cube of the diameter of each associated particle. Increasing reporter particle size can therefore be used to establish an affinity threshold favoring selection of individual aptamers capable of passing an operator-defined fitness test.

Single-molecule affinity selection can be achieved by immobilizing a target molecule to an SPM tip (i.e., negatively charged silicon nitride) used to probe a random-sequence, nanosphere-conjugated nucleic acid library. Scanning is performed in fluid mode to detect aptamer binding to the tip-immobilized target following application of the nucleic acid library sample to a freshly cleaved mica

substrate. The force of aptamer binding to the target-immobilized probe tip is quantified by varying loading and discharge forces associated with aptamer-nanoparticle binding and unbinding to target-probe tip. Individual, high-affinity aptamers are selected on quantitative grounds against an operator-defined binding force specification. See Paragraphs [0567] and [0568]

An aptamer may be a molecule unto itself or a sequence segment comprising a nucleotide molecule or group of molecules, e.g., a defined sequence segment or aptameric sequence comprising a synthetic heteropolymer, multivalent heteropolymeric hybrid structure or aptameric multimolecular device.

The term "structural molecules" refers to selected nonoligonucleotide molecules that may lack heretofore known specific binding or effector properties and includes, but is not limited to, selected molecules comprising structural shapes and surface features and selected molecules comprising elements, atoms, molecules, ions, and compounds comprising surfaces, amphibious surfaces, inorganic and organic materials such as carbon, silicon, glass, organic and inorganic crystals, selected solvents, selected solutes, natural, biomimetic and synthetic nanostructures and microstructures, fibers, filaments, silks, molecular scaffolds, nanotubes, nanorods, fullerenes, buckyballs, diamondoid molecules, semiconductors, insulators, metals, plastics, elastomers, polymers, detergents, lubricants, waxes, oils, powders, fillers, excipients, fibers, tableting ingredients, packaging materials, papers, industrial plastics, cyclic and polycyclic molecules, dendrons, dendrimers, electrolytes and polyelectrolytes, salts, hydrocarbons, ceramics and biological, biocompatible, biomimetic, biodegradable and

imprintable monomers, multimers and polymers, e.g., fatty acids, lipids, surfactants, amino acids, peptides, proteins, polyamines, polyacids, sugars, starches, cellulose, glycosylated molecules, glycopolymers and conjugates thereof. See Paragraph [0297]

When used in reference to single-molecule detection of an aptamer, "functional coupling" means to enable detection of an individual aptamer-target complex or multimolecular structure comprising a pair or group of molecules attached by nucleotides or, alternatively, to enable discrimination of an individual molecular complex or multimolecular structure from an uncomplexed nucleotide or nonnucleotide molecule or plurality of molecules. See Paragraph [0112]

Such functional coupling includes, for example, the participation of selected molecules or nucleic acid sequences as effector molecules, signal-generating molecules, donors or acceptors of mass (e.g., precursors, cofactors or products) or energy (e.g., electrons, photons, or radiationless transfer), reactants, substrates, cofactors, coenzymes, prosthetic groups, catalysts or intermediates in chemical or enzymatic reactions, including, electrochemical, photochemical and mechanochemical processes. See Paragraph [0517].

Therefore it would have been obvious to one of ordinary skill in the art that the method of dipping a scanning probe microscope tip in accordance with Mirkin (212) can be modified to use elastomer and electrochemical solutions according to the method of Cubicciotti (757), to coat the probe tip as recited in Claims 26 and 28.

Cubicciotti (757) also discloses that after application of adhesive(s) to

amphibious surface(s), the surface-bonding (i.e., adhesive) function can be willfully or environmentally triggered (i.e., initiated) by a first selected associative stimulus (i.e., an adhesive or bonding stimulus). Selected bonding stimuli include, for instance and without limitation, changes in ambient temperature, pressure, humidity or light exposure; the willful input or exchange of energy (e.g., laser light, photons, darkness, sound, heat, cold, electromagnetic radiation); or application or removal of a selected nonoligonucleotide molecule (e.g., a solvent, solute, ligand, receptor or effector molecule) or oligonucleotide (e.g., a linker oligonucleotide, aptamer or hybridizable defined sequence segment). The adhesives are also optionally reversible, preferably willfully or environmentally reversible, meaning that bonding can be reversed in response to a first dissociative selected stimulus (i.e., an unbonding or antiadhesive stimulus), as recited in Claim 24. Unbonding stimuli include, for instance and without limitation, changes in ambient temperature, pressure, humidity or light exposure and/or the willful input or exchange of energy, or application or removal of a selected nonoligonucleotide molecule or oligonucleotide. The unbonding stimulus may be the removal, absence or disappearance of the bonding stimulus (e.g., cooling, darkness, wetness or dryness). Alternatively, the unbonding stimulus may not be substantively different from the bonding stimulus (e.g., use of a solvent to unbond light-induced adhesion). Following unbonding, adhesion may optionally be restored, preferably by a second bonding stimulus and advantageously a repetition of the first bonding stimulus. See Paragraph [0502].

Conclusion

3. Any inquiry concerning this communication or earlier communications should be directed to Phillip Johnston whose telephone number is (703) 305-7022. The examiner can normally be reached on Monday-Friday from 7:30 am to 4:00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiners supervisor John Lee can be reached at (703) 308-4116. The fax phone numbers are (703) 872-9318 for regular response activity, and (703) 872-9319 for after-final responses. In addition the customer service fax number is (703) 872- 9317.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703 308 0956.

PJ

October 21, 2003